

Treatment of gonorrhoea with two oral doses of antibiotics

Trials of cephalexin and of triple tetracycline (Deteclo)

R. R. WILLCOX

St. Mary's Hospital, London, W.2

An efficient treatment for gonorrhoea using a single oral dose of medicament would have considerable advantages in the rapid handling of patients in venereal diseases clinics and also in the treatment of their contacts. Not only would such an oral method be less cumbersome but it would probably be preferred by most patients to injection. The full promise of such regimens of treatment using antibiotics has not yet been realized in terms of efficacy, toxicity, availability, or cost.

Although excellent results can confidently be expected with many antibiotics given by mouth in multiple dosage, this type of administration is not considered desirable because patients with venereal diseases often do not take their pills, capsules, or tablets at the times or in the doses suggested. They not infrequently cease to take tablets once their symptoms have abated but before a cure has been achieved and the drug may then be used for self-treatment on a later occasion or for sale on the black market.

Nevertheless all but a few patients can probably be trusted to take just one dose 4 to 6 hours after taking the first under supervision, in the clinic, and the present paper concerns the results obtained with two oral doses of two new drugs given in this way: a new orally-administered cephalosporin—cephalexin—and a newly-introduced triple tetracycline combination—'Deteclo'.

Cephalexin

This is a semi-synthetic analogue of cephalosporin C with a wide antibacterial activity which is greater *in vitro* against *Neisseria gonorrhoeae* than that of cephaloridine. It is supplied in black and orange capsules each of 500 mg. for oral administration. The antibiotic is rapidly absorbed and high serum levels

are obtained within 1 or 2 hours, but the fall off is such that 80 per cent. can be recovered from the urine within 6 hours (Foord, O'Callaghan, Muggleton, and Currie, 1969).

Single oral doses of 2 g. are unsuccessful in the treatment of gonorrhoea (Fowler, 1969; Oller and Smith, 1969), although better results can be obtained with single doses of 3 g. when probenecid is given in addition (Willcox and Woodcock, 1969).

When Fowler (1969) tried the double dose method by giving two oral doses each of 2 g. at an interval of 6 hours, he had a potential failure rate of 15 per cent. in 31 cases in males and no failures in 16 females treated, but he abandoned the treatment because of the difficulty of getting patients to attend twice on the same day. In the present trial, it was felt that patients could be trusted to take just one dose away from the clinic, and this report concerns the treatment of 102 male patients given two oral doses each of 2 g. cephalexin, the first being taken under supervision in the clinic and the second being handed to the patient to be taken after an interval of 5 hours.

CASE MATERIAL AND MANAGEMENT

Of the 102 male patients, all with uncomplicated gonorrhoea, 48 were born in the United Kingdom, 31 were Negroes (30 from the West Indies and one from Kenya), and the remainder were immigrants from other areas. Diagnosis was based on Gram-stained urethral smears and on cultures in some cases. At follow-up an examination was made of the urethra, with a smear (and culture in some cases) being taken if a discharge was present, and the urine was inspected for haze and threads. It was planned that patients should be seen at approximately 2 to 3 days, 7, 14, 28, 56, and 84 days after treatment and that at least one microscopic examination of the prostatic fluid should be made during this time.

FOLLOW-UP AND RESULTS (TABLE I)

Of the 82 patients followed, as judged by whether or not there was a history of further sexual intercourse, there were twelve failures all noted within 2 weeks (14.6 per cent.). If all recurrences noted within 2 weeks were counted as failures the rate would be 18.3 per cent. In spite of a substantially higher incidence of previous infections in the Negro patients, there was no higher recurrence rate in this group.

Apart from some difficulty experienced in swallowing the tablets, and their rejection by vomiting in one case no adverse effects were reported.

Triple tetracycline

A further series of 100 cases of uncomplicated gonorrhoea in men was treated with a new triple-tetracycline mixture, 'Deteclo'. Each patient was given two oral doses each of 1.2 g. (4 tablets) at an interval of 5 to 6 hours. Each 300-mg. blue tablet contained 69 mg. demethyltetracycline hydrochloride, 115.5 mg. chlortetracycline hydrochloride, and 115.5 mg. tetracycline hydrochloride.

CASE MATERIAL AND MANAGEMENT

Of the 100 male patients, fifty were born in the United Kingdom, 29 were Negroes (24 from the West Indies, two from East Africa, and one each from Columbia, Cuba, and U.S.A.), and 21 were immigrants from other areas. The management was on the same lines as in the previous series.

FOLLOW-UP AND RESULTS (TABLE II)

Of 89 patients followed, as judged by a previous history of further sexual exposures, there were eight cases of treatment failure (9 per cent.). If the calculation was based on all recurrences occurring within 2 weeks regardless of history, the figure would be only slightly smaller (8.9 per cent.). No significant difference was noted between Negro and other patients. Apart from nausea in one case no adverse side-effects were noted.

Comparison with other antibiotics

In Table III the results obtained with these two preparations are compared to those obtained under

TABLE I *Results with Cephalixin by two-dose method*

Duration of follow-up	No. followed	Results			
		Satisfactory	Non-gonococcal infection	Re-infection	Failure
0	102	—	—	—	1*
1-3 days	82	7	4	—	3
4-7 days	67	6	4	—	3
8-14 days	54	9	—	3	5
15-21 days	37	3	5	—	—
22-28 days	29	2	2	3	—
1-2 mths	22	2	4	4	—
2-3 mths	12	2	—	—	—
More than 3 mths	10	4	2	4	—
Total	82	35	21	14	12 (14.6 per cent.)

*Includes one man who vomited his first dose of tablets.

TABLE II *Results with Deteclo by two-dose method*

Duration of follow-up	No. followed	Results			
		Satisfactory	Non-gonococcal infection	Re-infection	Failure
0	100	—	—	—	—
1-3 days	89	13	2	—	1
4-7 days	73	15	1	1	4
8-14 days	52	4	1	—	1
15-21 days	46	3	—	1	1
22-28 days	41	—	2	2	1
1-2 mths	36	4	5	4	—
2-3 mths	23	3	—	2	—
Over 3 mths	18	11	1	6	—
Total	89	53	12	16	8 (9.0 per cent.)

TABLE III *Comparison with other antibiotics given in two doses*

Authors	Date	Antibiotic	Dose (g.)	No. of patients		Failures	
				Treated	Followed	No.	Per cent.
Willcox and Woodcock	1970	Cephalexin	2.0 + 2.0	102	82	12	14.6
Willcox	1965	Ampicillin	1.0 + 1.0	153	127	15	11.8
Willcox	1969a	Triple tetracycline	1.2 + 1.2	100	89	8	9.0
Willcox	1969b	Demethylchlortetracycline	1.2 + 1.2	107	93	4	4.3

like circumstances with two oral doses of two other antibiotics, and it is evident that the best results were given by demethylchlortetracycline.

Summary and conclusions

- (1) The oral treatment of gonorrhoea is considered and the results obtained using two oral doses of two newly-introduced antibiotic preparations are described.
- (2) 102 male patients were treated with two oral doses each of 2 g. cephalixin—a new semi-synthetic cephalosporin antibiotic. Among 82 cases followed there were twelve supposed failures (14.6 per cent.).
- (3) A further 100 patients were given two doses each of 1.2 g. of a combination of three established tetracycline antibiotics available in a single tablet. Among 89 cases followed there were eight supposed failures (9 per cent.).
- (4) These results are compared with those previously obtained with two oral doses of ampicillin and of

demethylchlortetracycline. The best results were obtained with the latter, which yielded a failure rate of only 4.3 per cent.

Grateful acknowledgements are expressed to Glaxo Laboratories Ltd. for kindly providing the 'Ceporex' and to Lederle Laboratories Ltd. for the 'Deteclo' used in this study.

References

- FOORD, R. D., O'CALLAGHAN, C. H., MUGGLETON, P. W., and CURRIE, J. P. (1969) "Proc. Symposium on The Clinical Evaluation of Cephalexin," Royal Soc. Med., London, June, 1969, ed. R. D. Foord, pp. 3-6. Glaxo Laboratories, Greenford, Middlesex
- FOWLER, W. (1969) *Ibid.*, pp. 54-56
- OLLER, L. Z., and SMITH, H. C. (1969) *Ibid.*, pp. 51-54
- WILLCOX, R. R. (1965) *Brit. J. clin. Pract.*, **19**, 689
- (1969a) *Clin. Trials J.*, **6**, 152
- (1969b) *Acta derm.-venereol. (Stockh.)*, **49**, 103
- and WOODCOCK, K. (1970) *Postgrad. med. J.*, **46**, Suppl. (October), p. 103